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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
1655	23

DATE MAILED: 12/19/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/341,227	DURR ET AL.	
	Examiner	Art Unit	
	Bradley L. Sisson	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 August 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 27 September 2001 has been entered.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The use of the trademark NONIDET P-40 (NP-40) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The quantity of experimentation need is great, on the order of several man-years and then with little, if any, reasonable expectation of success.

The Amount of Direction or Guidance Provided and The Presence or Absence of Working Examples

The amount of guidance provided is scant. Upon review of the disclosure the following examples have been found:

a) Electrokinetic injection of nucleic acid using a quartz capillary having a 50-micrometer internal diameter (page 20);

b) Size-exclusion recovery rate (pages 21-22);

c) Nucleic acid extraction (pages 22-23);

d) Nucleic acid concentration (pages 23-24);

e) Derivatization of nucleic acids on memfil PCTE 10 nm membrane (page 24); and

f) Coupling with electron microscopy (pages 24-25).

The disclosure has not been found to provide enabling guidance for the analysis of any molecules other than the isolated plasmid DNA used in the above-identified examples.

The Nature of the Invention

The claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The state of the prior art is one of continuing development and interest. While the art allows for the immobilization of a variety of purified macromolecules under chromatography, as well as large-scale gel electrophoresis of proteins and nucleic acids, the ability to analyze any and all types of macromolecules via electrokinetic manipulation is far from routine.

The Relative Skill of Those in the Art

The relative skill of those in the art that is most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

The Breadth of Scope of the Claims

The claims have sufficient breadth of scope so to encompass performing any one or combination of analytical methods on virtually compound or composition of matter. In support of this position it is noted that claim 14 further defines the "macromolecules" of claim 13 as being the life forms of "bacteria or fungi." In view of such a definition, the "macromolecule" of claim 13 has been interpreted as encompassing any composition of matter, organic in nature or otherwise.

In order for one of skill in the relevant art (at the time the invention was made) to practice the invention to the full scope of each claim, said skilled artisan would have to resort to determine parameters such as how to manufacture any number of varied devices that comprises any number of microchannels of virtually any diameter and are placed in any substrate, including that which may react with components of the "macromolecule" and where the substrate is not translucent, and where the microchannels may comprise branch points. The method also encompasses performing virtually any one or plurality of analysis methodologies where the "macromolecule" can be any compound or composition, *supra*.

The disclosure has been found to provide examples whereby purified plasmid DNA was used under set conditions. No other compound or macromolecule, much less a composition of macromolecules, have been exemplified. While it is not a requirement that applicant set forth an

example of each and every possible embodiment encompassed by the claims, the disclosure does need to fully enable each and every aspect of its scope. The claimed invention is drawn to chemical analytical methodologies, which, as evidenced by the type of "macromolecule" encompass the physiological aspects of various life forms. Both chemical reactions and physiological systems are recognized as being unpredictable and as such require greater levels of disclosure. *In re Fisher.*

It is apparent that at least some of the claims embody a method whereby a macromolecule is trapped on a membrane. It is noted that the membrane is to be located within the lumen of the microchannels. The disclosure does not set forth a reproducible method whereby any membrane can be inserted into a microchannel of virtually any diameter, much less allow for the further characterization of any and all possible "macromolecules" trapped or bound thereon or therein. Seemingly the skilled artisan would need to be able to extricate the micromembrane from the microchannels, yet the specification is silent as to how such a step is to be performed. Absent some step whereby the membrane is removed from each of the hundreds of microchannels (see claim 18 where it is indicated that the device can comprise up to 400 such microchannels or capillaries) the skilled artisan must then be able to perform any and all analytical steps with the "macromolecule" remaining in the microchannel with the membrane. The specification does not set forth a repeatable procedure whereby any macromolecule is retained in the hundreds of microchannels is analyzed wherein said microchannels take on any conformation and are found in a substrate that can be made of any composition.

The claims are also considered to encompass the application of an electrokinetic force yet the device described in the claims does not recite any elements that would allow for the

application of such a force. The specification has not set forth a reproducible procedure whereby an electrokinetic force would be applied when the device is void of any means to provide for such.

The method and device claims do not recite any means or steps whereby the result of any analytical method is detected and correlated with any results obtained. The specification has not set forth a reproducible method whereby any analytical methodology can be performed in the absence of some detection and correlation step(s).

The failure of the specification to fully enable the full scope of protection sought by the claims now before the Office would require the skilled artisan to resort to determining how each embodiment of the invention is to be practiced and what operational limitation exist. Such non-enablement by applicant unfairly shifts the burden to that of the public. While some experimentation is permitted, the level of experimentation needed so to fully enable the scope of the claims rises to the level of undue experimentation. *Genentech v. Novo Nordisk A/*S 42 USQP2d 1001. In view of the breadth of scope clamed, the limited guidance provided, the unpredictable nature of the art to which the claimed invention is directed, and in the absence of convincing evidence to the contrary, the claims are not enabled by the disclosure.

Response to argument

Argument is presented in the response of 27 September 2001 that the claimed invention is not directed to unpredictable factors found in chemistry and physiology but are directed instead to "more predictable physical parameters" (page 6, last paragraph, of the response). This argument ahs been fully considered and has not been found persuasive. It is noted with

particularity that the claims are drawn to a method of analyzing any type of "macromolecule" which can and does include life forms. Further, the claims are not limited to any type of analysis. While agreement is reached in that the claims do indicate that there is a "collection of macromolecules on a membrane" (claim 1), such a step is prior to the analysis, the object of the claim. The analytical aspect is considered to be chemical. Further, the analysis of life forms is considered to encompass physiological conditions.

Argument is also advanced as to the specification being enabling and that the level of experimentation required to enable the claims does not rise to the level of undue experimentation. This argument has been fully considered and has not been found persuasive. As presented in pages 5-7 above, the Office has set forth reason as to why the specification of the subject application is not enabling. Accordingly, and in the absence of convincing evidence to the contrary, the rejection is maintained.

Applicant, at page 8 of the response, questions why claims 17, 23, and 28, which require the macromolecule to be nucleic acid, are not enabled by the disclosure. In response to this inquiry it is noted that there is no requirement that the nucleic acid be in a purified state and that the nucleic acid can be located within viable cells or tissue. The claims, as indicated above and below, fail to recite any method steps directed to just how the analysis is to be performed. Consequently, the claims have been interpreted as encompassing performing any and all manner of analysis on nucleic acids. Similarly, there is no limitation placed on the size, conformation, and reactive properties of the microchannels, nor for the substrate in which they are found. The specification has not set forth a repeatable procedure whereby any and all manner of microchannels, using any membrane under any conditions, allow for the analysis of any nucleic

acid, or mixture thereof. At best the specification has been found to provide a general suggestion as to where others may explore and develop the concept presented by applicant. To the extent that the specification teaches or recites certain limitations, it is noted that limitations found within the specification are not read into the claims.

While agreement is reached in that applicant is entitled to claim their invention as broadly as possible (see response at page 9, second paragraph), the specification must also fully enable the scope of protection sought. Absent full enablement of scope, narrowing of claims is suggested as a means by which the rejection may be overcome.

Claims 18 and 19 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification fails to set forth in sufficient detail a device that permits any form of analysis of any and all possible "macromolecules." As set forth in claim 18, the device is to comprise a chip and from 1 to 400 capillaries with an embedded membrane. The specification does not provide an adequate written description of a device, nor methods for its manufacture and use. As presently claimed, the device does not have any means for introducing the sample, for processing the sample, nor for the removal of any macromolecules that has become entrapped on the membrane. Further, the claims and specification do not describe in sufficient detail, or enable, a device that lacks means for electrokinetic movement. As a result of the deficiencies of the specification in describing the claimed device, the subject application dos not reasonably suggest that applicant was in

possession of the full scope of devices claimed. In support of this position, attention is directed to the decision of *Vas-Cath Inc. v. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

For the above reasons, and in the absence f convi9ncing evidence to the contrary, the specification not been found to adequately describe the claimed device such that the written description requirement if 35 USC 112, first paragraph has been satisfied.

Response to argument

Applicant, at page 10 of the response, asserts that the specification does adequately describe the claimed device as not claimed, noting the amendment to claim 18.

The above argument has been fully considered and has not been found persuasive towards the withdrawal of the rejection. While agreement is reached in that the claims require the 1 to 400 capillaries to be "side-by-side" to one another, the specification does not support the position that a device of 1 to 400 microchannels has been developed where the diameter of the microchannel can be of any diameter and of any length, and are formed in a substrate of any width. In support of this position attention is directed to page 8 of the disclosure where it is indicted that the microchannels can range in size of from 10-100 μm. It is also plainly evident from reading said passage that the "entire module is thus 3 to 10 cm long, 1 to 50 mm wide and 0.1 to 50 mm thick." As presently worded, however, the claims are not limited to such

disclosures and the limitations found within the specification and such limitations have not been read into the claims.

As a requirement of claims 18 and 19 the device is to comprise a membrane within the "capillaries." For purposes of examination the "capillaries" have been considered to be the same as the "microchannels" of claim 1. Further, the aspect of the "embedded membrane" requires the membrane to have been physically inserted within the lumen of each capillary or microchannel as found represented by element (2) in Figures 1-5, and not sandwiched between different blocks as represented by element (2) in Figures 6-8. The specification has not been found to provide an adequate written description of embedding any membrane in any microchannel.

For the above reasons, and in the absence of convincing evidence to the contrary, the specification has not been found to satisfy the written description requirement for claims 18 and 19.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. This claim is an omnibus type claim. A review of the claims finds a characterization in some instances of the device used in their collection and at time a method step used in their collection but all steps recited are

preliminary to any analysis. The method claims have not been found to recite any method steps by which the "analysis" is to be performed. Consequently, the method of "analyzing" by "analyzing" does not adequately describe the method steps needed to practice the claimed method. Claims 18 and 19, drawn to a device to be sued in the method do not overcome this issue and are similarly rejected.

Claim 16 is confusing as to whether the "MS, gel electrophoresis, PCR, TEM, nucleic acid sequencing, immunodiagnosis or hybridization" are to be part of the "analysis" or operations that are to be performed prior or subsequent to said analysis.

Claims 18-23 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: Means that allow for electrokinetic collection of nucleic acids on the membrane. As presently worded the device of claims 18 and 19 lacks any electrical connections yet the method of claim 20, and claims 21-23 which depend therefrom, require there be performed an electrokinetic collection of nucleic acids.

Response to argument

At pages 11-12 of the response it is asserted that the rejection of claims under 35 USC 112, second paragraph, for missing essential elements is improper as it should be made under 35 USC 112, first paragraph. This argument has not been found to be persuasive towards the withdrawal of the rejection. A claim that that lacks essential elements can be rejected under 35 USC 112, second paragraph, to the extent that it is incomplete and that applicant has not claimed the invention. At the same time that the claim is rejected under 35 USC 112, second paragraph,

an additional rejection "may" also be made under 35 USC 112, first paragraph, as the specification does not enable the use of an invention that lacks these essential and missing elements.

Acknowledgement is made of applicant's amendment to the preamble of the claims. And acknowledgement is made of applicant's argument at page 12, last paragraph, that the amendment "makes clear that the claimed devices are 'for use in performing the method of claim 13.'" The aspect that the preamble of a product claim has been amended has not been found dispositive of the instant rejection as the preamble of such a claim is not considered to be limiting. Further to the point, it is stated at page 13, penultimate paragraph, "that Applicant did not narrow the claims in any material respect."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-16 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Tomlinson et al.

Tomlinson et al., disclose a method of analyzing peptide mixtures via capillary electrophoresis wherein the device comprises a membrane that spans the lumen of the capillary. This meets a limitation of each of claims 13-16 and 29.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is 703-308-3978. The examiner can normally be reached on Monday through Thursday from 6:30 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 703-308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

B. L. Sisson

Bradley L. Sisson
Primary Examiner
Art Unit 1655

BLS
December 15, 2001